REMARKS

Formal Matters

Claims 1-33 were pending in the application and were restricted into eight groups. Claims 1-11, 15, 19-30 and 32 are canceled. As discussed below, Applicants elect with traverse claims 12-14, 16-18, 31, and 33 (Group IV). Claims 12-14, 16, 31 and 33 are amended and claims 34-38 are added. No new matter is added by the amendments to the claims.

Support for the amendments is found throughout the specification such as at, for example, page 11, lines 23-25; page 11, line 27 to page 12, line 7; page 12, line 22 to page 13, line 2; page 13, lines 3-21; page 19, lines 22-23 (legend to Fig. 8) and Fig. 8; page 20, lines 17-22; page 22, line 15 to page 23, line 17; page 97, line 14 to page 98, line 7 and Fig. 4; and page 100, lines 5-10, Fig. 8, and Table 5 (page 100). No new matter is added by the amendments to the claims.

Sequence Rules

Applicants are required to comply with the sequence rules as set forth in 37 C.F.R. § 1.821-25 at the time of election of the restriction. Applicants believe that they have already complied with 37 C.F.R. § 1.821-25 by submitting a Letter and Request to Use Computer-Readable Sequence Listing Under 37 CFR § 1.821(e) upon filing the instant application on March 7, 2000 (copy of Letter enclosed). Specifically, the Letter requested that the computer-readable Sequence Listing filed in parent application Serial No. 09/070,416 be used as the computer-readable Sequence Listing for the instant application. A paper copy of the Sequence Listing and a statement that it is identical to the computer-readable copy from Serial No. 09/070,416 under 37 CFR § 1.821(e) was submitted with the Letter.

Applicants herewith submit another copy of the Sequence Listing for the convenience of the Examiner and in the unlikely circumstance that the

Applicants submit a copy of the Letter and Request and 37 CFR § 1.821(e), another paper copy of the Sequence Listing, and state that the computer readable copy and paper copy are identical, that no new matter is added by the amendment. As a result, Applicants believe that they have complied with the Notice to Comply.

Correction of Inadvertent Omission from the Specification When Filed

Upon filing the instant specification as a continuation of parent application 09/070,416 and provisional application serial no. 60/050,661, Appendix I was inadvertently omitted. Appendix I is a 15-page table comparing sequence identities between various light chain sequences. Insertion of the table into the specification does not add new matter because the table was present in the provisional application 60/050,661 to which the present application ultimately claims priority. Insertion of the Appendix as Table 6.1-6.15 is respectfully requested.

In a related application, U.S. application serial no. 08/850,058, the position of Appendix I was objected to. Appendix I was after "What is claimed is:" on page 103 and before the Claims. Applicants renamed the table as Table 6.1-6.15 and repositioned it to immediately before "What is claimed is:". Applicants respectfully offer this positioning scheme for consideration in the instant application.

Applicants submit Table 6.1-6.15 on fifteen pages. The word "Appendix" and the original page number on each page of the original appendix are deleted and "Table 6.X" is inserted therefor, where "X" refers to subpart 1-15 of Table 6.

The word "Appendix" occurs only once in the originally filed specification at page 96, line 24. The word "Appendix" has been deleted from the specification and the term "Table 6.1-6.15" has been inserted therefor.

No new matter has been added by these amendments to the

Other Amendments to the Specification

Applicants amended the specification on page 13, line 27 to correct a typographical error by replacing a semicolon (";") with a period (".") . No new matter was added by the amendment to the specification.

Applicants amended the specification to correct a typographical error in the legend for Fig. 2A-2C on page 17, line 30. Specifically, Fig. 2C shows the sequence of a portion of the nucleic acid construct depicted in Fig. 2B. Originally filed Fig. 2C indicates that that sequence is SEQ ID NO:13 and thus provides support for the amendment. Correction of the legend for Fig. 2C has been corrected accordingly. No new matter has been added by the amendment to the specification.

Election/Restriction

The Examiner has indicated that the application contains claims directed to patentably distinct species of the claimed invention and requires restriction under 35 U.S.C. § 121 according to the eight groupings indicated in the Office Action (Paper No. 4, mailed July 5, 2001)

In addition, Applicants were asked to further elect patentably distinct species of the claimed invention as indicated on page 4 of the Office Action. Applicants elect with traverse, for the reasons stated herein, the following species:

The constant domain is from a human IgG.

The anti-Ob-R/anti-HER3 species.

Applicant respectfully traverses the restriction and election requirement as applied to the currently pending claims for the reasons provided below.

Applicant respectfully traverses the restriction requirement in which free thiol or protuberance/cavity structures within the [illegible] as the basis for the support the restriction. The

[illegible]

class 530 and subclass 387.3 as another multispecific antibody of the invention comprising a protuberance and cavity in the multimerization domain (Group IV). Thus, the Examiner would not be placed under an undue burden to search in the same class and subclass of art in order to evaluate the patentability of claims in Groups III and IV, for example. The same argument applies to Groups I and II, Groups V and VI, and Groups VII and VIII. Applicants respectfully submit that the restrictions that distinguish Group I from Group II, Group III from Group IV, Group V from Group IV, and Group IV from Group VIII should be withdrawn.

Without acquiescing to the restrictions, however, and merely to expedite prosecution of the claims, Applicants elect with traverse Group IV, Claims 12-14, 16-18, 31 and 33 drawn to a multispecific antibody, wherein the multimerization domain is altered to comprise a protuberance and a cavity.

With respect to the election of species requirement, Applicants respectfully traverse the election requirement for failing to recognize Applicant's right to allowed claims that link a reasonable number of species under 37 CFR § 1.141. It is Applicant's understanding and right under 37 CFR § 1.141 that, following election, the claims will be examined fully with respect to the elected species and further to the extent necessary to determine patentability for a reasonable number of species encompassed by the generic claims.

With the above reservation of right, Applicant elects, with traverse, a constant domain from a human IgG and further elects anti-Ob-R/anti-HER3, an illustrative example of the claimed multispecific antibody of the invention.

A marked-up version and a clean version of the pending claims is attached.

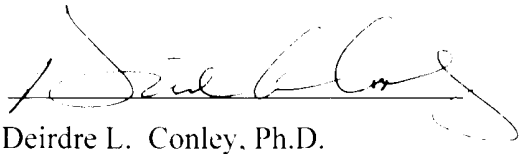
If the Examiner has any questions, the Examiner should feel free to call the undersigned attorney at the number indicated below.

This document is timely filed with a petition and fees for a three-month extension of time. In the unlikely event that additional fees are due, Applicants hereby petition the Commissioner to authorize any extensions of time and/or to deduct fees from or add credits to our Deposit Account 07-0630 as necessary to maintain the pendency of this application.

Respectfully submitted,

GENENTECH, INC.

Date: November 5, 2001

By: 

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PATENT TRADEMARK OFFICE

Doc. #99911

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

Deleted information is shown in strikethrough (~~θ~~), and added information is shown as underlined.

Paragraph beginning at page 13, line 26, has been amended as follows:

(ii) recovering the multispecific antibody from the host cell culture;.

Paragraph beginning at page 17, line 16, has been amended as follows:

Figs. 2A-2C. Fig. 2A diagrams a selection scheme for C_H3 heterodimer using phage display vector, pRA2. Phage displaying stable C_H3 heterodimers are captured using an antibody directed to the gD flag. Fig. 2B diagrams a dicistronic operon in which C_H3 expressed from a synthetic gene is co-secreted with a second copy of C_H3 expressed from the natural gene (Ellison et al. Nucleic Acids Res. 10:4071-4079 (1982)) as a fusion protein with M13 gene III protein. The synthetic C_H3 gene is preceded by a sequence encoding a peptide derived from herpes simplex virus glycoprotein D (gD flag, Lasky, L. A. and Dowbenko, D. J. (1984) DNA 3:23-29; Berman, P. W. *et al.*, (1985) Science 227:1490-1492 and a cleavage (G) site for the site-specific protease, Genenase I (Carter, P. *et al.* (1989) Proteins: Structure, Function and Genetics 6:240-248). Fig. 2C is the nucleic acid sequence of the dicistronic operon ~~(SEQ ID NO:1)~~ (SEQ ID NO: 13) of Fig. 2B in which the residues in the translated C_H3 genes are numbered according to the

gene (366, 368, and 407).

Paragraph beginning at page 96, line 8, has been amended as follows:

--A large human single chain Fv (scFv) antibody library (Vaughan *et al.* (1996), *supra*) was panned for antibodies specific for eleven antigens including Axl(human receptor tyrosine kinase ECD), GCSF-R (human granulocyte colony stimulating factor receptor ECD), IgE (murine IgE), IgE-R (human IgE receptor α-chain), MPL (human thrombopoietin receptor tyrosine kinase ECD), MusK (human muscle specific receptor tyrosine kinase ECD), NpoR (human orphan receptor NpoR ECD), Rse (human receptor tyrosine kinase, Rse, ECD), HER3 (human receptor tyrosine kinase HER3/c-erbB3 ECD), Ob-R (human leptin receptor ECD), and VEGF (human vascular endothelial growth factor) where ECD refers to the extracellular domain. The nucleotide sequence data for scFv fragments from populations of antibodies raised to each antigen was translated to derive corresponding protein sequences. The V_L sequences were then compared using the program "align" with the algorithm of Feng and Doolittle (1985, 1987, 1990) to calculate the percentage identity between all pairwise combinations of chains (Feng, D.F. and Doolittle, R.F. (1985) J. Mol. Evol. 21:112-123; Feng, D.F. and Doolittle, R.F. (1987) J. Mol. Evol. 25:351-360; and Feng, D.F. and Doolittle, R.F. (1990) Methods Enzymol. 183:375-387). The percent sequence identity results of each pairwise light chain amino acid sequence comparison were arranged in matrix format ~~(Appendix)~~ Table 6.1-6.15).

The Appendix is amended to become Table 6.1-6.15 as follows:

							Axl											GCSFi					
	Clone	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
1	Axl.25	-	49	50	81	83	79	83	46	49	49	90	45	80	46	48	42	43	44	49	50	50	79	49
2	Axl.26		-	98	48	52	47	52	70	77	71	49	68	47	68	72	57	58	59	71	97	98	47	71
3	Axl.27			-	49	53	48	53	72	79	73	50	70	48	69	74	59	60	61	73	99	100	48	73
4	Axl.32				-	82	83	83	48	49	46	85	45	84	44	48	42	42	44	46	49	49	98	48
5	Axl.35					-	77	100	48	52	52	84	51	78	49	52	46	47	48	52	53	53	80	53
6	Axl.36						-	78	48	48	47	85	47	99	44	47	42	42	43	47	48	48	81	49
7	Axl.47							-	48	52	52	84	51	79	49	52	46	47	48	52	53	53	81	53
8	Axl.51								-	72	64	49	61	48	60	66	57	57	58	64	71	72	47	69
9	Axl.75									-	66	50	60	48	62	65	61	60	63	66	78	79	48	67
10	Axl.78										-	48	85	47	95	90	59	58	61	100	72	73	45	94
11	Axl.80											-	47	85	45	49	43	44	45	48	50	50	84	50
12	Axl.82												-	47	80	83	60	58	62	85	69	70	44	82
13	GCSFR.3.2E.A1													-	44	47	42	42	43	47	48	48	82	49
14	GCSFR.3.2E.D5														-	87	57	56	58	95	68	69	43	90
15	GCSFR.3.2E.D6															-	60	60	62	90	73	74	47	90
16	GCSFR.3.2E.G5																-	90	98	59	58	59	42	59
17	GCSFR.3.3E.C4																	-	91	58	59	60	42	58
18	GCSFR.A2																		-		60	61	43	61
19	GCSFR.A4																				72	73	45	94
20	GCSFR.A5																				-	99	48	72
21	GCSFR.A8																					-	48	73
22	GCSFR.F7																						-	47
23	GCSFR.G3																							-
24	IgE.D8																							
25	IgE.G2																							
26	IgER.1A12																							
27	IgER.1D11																							
28	IgER.1E10																							
29	IgER.MAT2C1G11																							
30	Mpl.01																							
31	Mpl.02																							
32	Mpl.03																							
33	Mpl.04																							
34	Mpl.05																							
35	Mpl.06																							
36	Mpl.07																							
37	Mpl.08																							
38	Mpl.11																							
39	Mpl.12																							
40	Mpl.14																							

41	Mpl.16
42	Mpl.19
43	Mpl.21
44	Mpl.24
45	Mpl.26
46	Mpl.28
47	Mpl.29
48	Mpl.30
49	Mpl.31
50	Mpl.32
51	Mpl.33
52	Mpl.35
53	MusK.01
54	MusK.02
55	MusK.06
56	NpoR.25
57	NpoR.44
58	NpoR.53
59	NpoR.81
60	NpoR.86
61	Rse.01
62	Rse.02
63	Rse.03
64	Rse.04
65	Rse.07
66	Rse.08
67	Rse.15
68	Rse.16
69	Rse.18
70	Rse.20
71	Rse.21
72	Rse.22
73	Rse.23
74	Rse.24
75	Rse.52
76	Rse.53
77	Rse.58
78	Rse.60
79	Rse.61
80	Rse.63
81	her3.1
82	her3.10

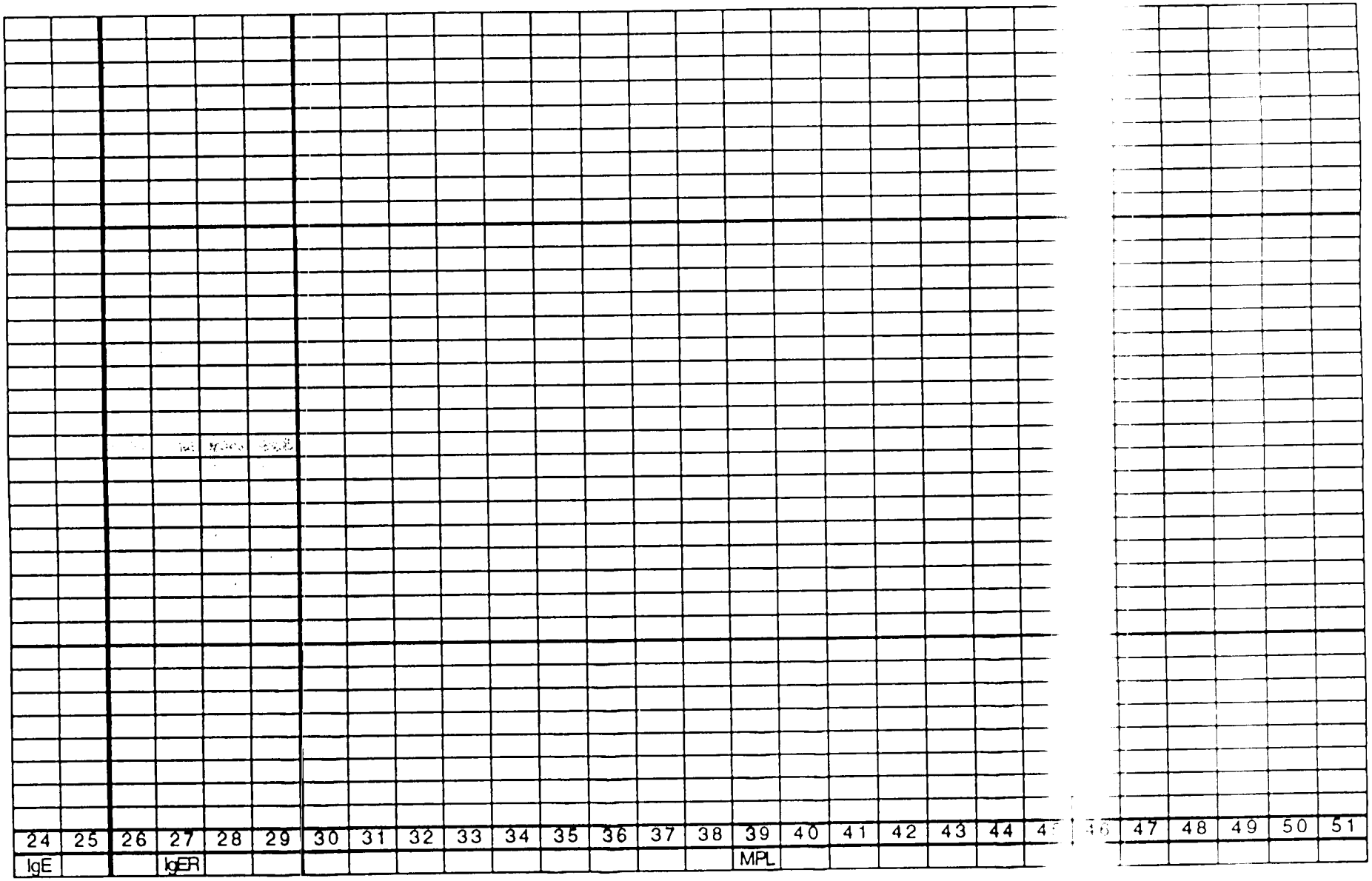
83	her3.11																							
84	her3.12																							
85	her3.16																							
86	her3.18																							
87	her3.19																							
88	her3.22																							
89	her3.3																							
90	her3.4																							
91	her3.7																							
92	obr.1																							
93	obr.11																							
94	obr.12																							
95	obr.14																							
96	obr.15																							
97	obr.16																							
98	obr.17																							
99	obr.18																							
100	obr.19																							
101	obr.2																							
102	obr.20																							
103	obr.21																							
104	obr.22																							
105	obr.23																							
106	obr.24																							
107	obr.26																							
108	obr.3																							
109	obr.4																							
110	vegf.1																							
111	vegf.10																							
112	vegf.2																							
113	vegf.3																							
114	vegf.4																							
115	vegf.5																							
116	vegf.6																							
117	vegf.8																							
	Clone	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
							Axl																	

APPENDIX ~~5~~ Table 6.3

IgE			IgER												MPL											
24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45		47	48	49	50	51
44	80	44	48	44	49	46	44	46	79	50	100	51	49	79	78	81	81	49	80	80	50		43	45	46	47	47
59	47	59	66	58	71	58	57	57	47	66	50	76	68	48	43	48	48	68	47	48	70		65	72	73	69	63
61	48	61	68	60	73	60	59	59	48	68	50	77	70	49	44	49	49	70	48	49	72		66	74	75	70	65
44	84	44	46	44	46	46	42	45	83	48	81	50	46	83	80	100	100	45	84	83	47		45	46	47	47	44
48	78	48	52	48	52	48	45	48	78	53	83	55	52	78	76	82	82	51	78	78	53		49	48	49	50	51
43	98	43	48	43	47	45	43	44	98	47	79	48	47	94	95	83	82	46	99	99	48		43	46	47	45	46
48	79	48	52	48	52	50	47	49	78	53	83	53	52	78	75	83	82	51	79	78	53		47	48	49	49	50
58	48	58	62	57	64	57	55	56	48	62	47	74	64	47	44	48	48	65	48	49	63		73	80	80	76	60
63	49	63	64	62	66	62	58	61	48	64	50	78	68	48	44	49	49	68	48	49	65		68	74	75	72	61
61	47	61	80	60	100	60	57	59	47	79	50	66	84	48	43	46	46	83	47	48	97		61	65	66	65	79
45	85	45	48	45	48	47	45	47	85	49	90	52	48	83	84	85	86	47	85	86	49		45	47	48	49	47
62	47	62	74	61	85	61	56	60	47	74	46	62	75	47	43	45	45	75	47	48	85		60	61	62	64	72
43	99	43	48	43	47	45	43	44	99	47	80	48	47	95	96	84	83	46	100	100	48		43	46	47	45	46
58	44	58	76	57	95	57	54	56	44	75	47	63	79	45	41	44	44	79	44	45	92		57	60	61	61	74
62	47	62	76	61	90	61	58	60	47	76	49	67	79	48	43	48	48	79	47	48	89		62	64	65	65	74
98	42	98	59	97	59	97	87	98	42	71	43	65	57	42	38	42	42	60	42	42	59		52	57	58	59	55
91	42	91	57	90	58	90	97	91	42	66	44	64	55	42	38	42	42	57	42	42	58		51	57	58	57	52
100	43	100	61	99	61	99	88	100	43	72	45	67	59	44	40	44	44	62	43	44	61		54	59	60	61	57
61	47	61	80	60	100	60	57	59	47	79	50	66	84	48	43	46	46	83	47	48	97		61	65	66	65	79
60	48	60	67	59	72	60	59	59	48	68	50	77	70	49	44	49	49	69	48	49	71		66	73	74	70	65
61	48	61	68	60	73	60	59	59	48	68	50	77	70	49	44	49	49	70	48	49	72		66	74	75	70	65
43	82	43	45	43	45	45	41	44	81	47	79	49	45	81	78	98	97	44	82	81	46		44	45	46	46	43
61	49	61	75	60	94	60	57	59	49	74	50	67	78	50	45	48	48	79	49	50	93		64	70	70	68	73
-	43	100	61	99	61	99	88	100	43	72	45	67	59	44	40	44	44	62	43	44	61		54	59	60	61	57
	-	43	48	43	47	45	43	44	98	47	80	48	47	94	95	84	83	46	99	99	48		43	46	47	45	46
		-	61	99	61	99	88	100	43	72	45	67	59	44	40	44	44	62	43	44	61		54	59	60	61	57
			-	60	80	60	55	59	48	85	49	65	94	48	44	46	46	93	48	49	78		58	60	60	61	99
				-	60	98	87	99	43	71	45	67	58	44	40	44	44	61	43	44	60		53	58	59	60	56
					-	60	57	59	47	79	50	66	84	48	43	46	46	83	47	48	97		61	65	66	65	79
						-	87	99	45	75	46	67	61	45	41	46	44	61	45	44	60		55	58	59	60	57
							-	88	43	67	44	63	56	43	39	42	40	56	43	42	57		51	56	57	55	52
								-	44	74	46	68	60	44	42	45	44	60	44	44	59		55	57	58	60	58
									-	47	80	48	47	94	95	83	83	46	99	100	48		43	46	47	45	46
										-	50	75	82	47	43	48	48	80	47	48	76		64	62	63	66	84
											-	51	50	79	78	81	81	50	80	80	50		43	46	47	48	47
												-	70	47	46	50	51	69	48	49	65		74	72	73	75	64
													-	47	43	46	46	97	47	48	81		62	63	64	64	93
														-	91	83	83	47	95	96	49		42	46	47	47	45
															-	80	81	42	96	98	44		40	42	43	43	46
																-	100	45	84	83	47		45	46	47	47	44

-	45	83	83	47	47
	-	46	47	80	61
		-	100	48	43
			-	49	44
				-	64
					45
					-

46	47	48	45	
63	64	64	92	
46	47	45	46	
47	48	47	48	
64	65	68	76	
46	47	47	44	
74	74	93	57	
-	99	77	57	
	-	78	58	
		-	60	
			-	



APPENDIX ~~6~~ Table 6.6

	MusK					NpoR												Rse									
52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73		5	76	77	78	79
79	80	79	81	81	44	45	45	80	46	46	46	48	72	81	49	46	47	47	45	81	49		51	49	44	46	100
47	47	47	48	50	59	46	45	47	73	73	71	70	42	48	71	69	71	70	70	48	71		83	94	59	73	49
48	48	48	49	51	61	47	46	48	75	75	73	72	43	49	73	71	73	71	72	49	73		85	96	61	75	50
83	84	83	100	81	44	48	46	84	47	47	46	45	88	100	46	43	47	44	45	100	46		49	49	44	47	81
77	78	77	82	79	48	48	47	78	49	49	51	51	80	82	52	48	52	50	50	82	52		55	52	48	49	83
98	99	98	83	76	43	46	44	99	47	47	47	46	73	83	47	43	48	45	46	83	47		49	48	43	47	79
78	79	78	83	80	48	48	46	79	49	49	51	51	74	83	52	48	52	50	50	83	52		55	52	48	49	83
48	48	48	48	49	58	44	44	48	80	80	65	63	41	48	64	60	67	62	64	48	64		68	76	58	80	46
48	48	48	49	51	63	46	48	48	75	75	66	65	42	49	66	61	66	64	65	49	66		74	75	63	75	49
47	47	47	46	49	61	48	47	47	66	66	89	99	41	46	100	95	90	98	88	46	100		83	73	61	66	49
85	85	85	85	81	45	46	46	85	48	48	47	47	77	85	48	45	48	46	46	85	48		51	50	45	48	90
47	47	47	45	47	62	45	46	47	62	62	80	84	40	45	85	84	81	83	79	45	85		77	70	62	62	45
99	100	99	84	77	43	46	44	100	47	47	47	46	74	84	47	43	48	45	46	84	47		49	48	43	47	80
44	44	44	44	46	58	46	45	44	61	61	84	94	40	44	95	90	86	93	86	44	95		78	69	58	61	46
47	47	47	48	50	62	50	49	47	65	65	88	89	42	48	90	86	89	88	88	48	90		89	76	62	65	48
41	42	41	42	44	98	47	46	42	57	58	58	58	38	42	59	52	59	57	57	42	59		62	57	98	58	42
41	42	41	42	43	91	48	49	42	57	58	57	57	38	42	58	52	58	57	57	42	58		62	58	91	58	43
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82	83	82	100	80	44	43	47	83	47	47	46	45	94	100	46	43	47	44	45	100	46	[illegible]	49	49	44	47	81
46	46	46	45	51	62	43	45	46	64	64	75	82	40	45	83	82	76	81	74	45	83	[illegible]	73	70	62	64	49
99	100	99	84	77	43	46	44	100	47	47	47	46	74	84	47	43	48	45	46	84	47	[illegible]	49	48	43	47	80
99	100	99	83	76	44	47	46	100	48	48	48	47	78	83	48	43	49	46	47	83	48	[illegible]	50	49	44	48	80
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82	83	82	99	80	44	48	46	83	47	47	46	45	87	99	46	43	47	44	45	99	46	[illegible]	49	49	44	47	80
43	43	43	45	47	54	39	38	43	74	74	60	60	45	45	61	62	61	59	60	45	61	[illegible]	66	68	54	74	43
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47	47	47	47	49	60	47	46	47	100	100	67	65	42	47	66	60	68	64	66	47	66	[illegible]	67	79	60	100	46
45	45	45	47	49	61	44	45	45	77	78	64	64	43	47	65	61	65	63	64	47	65	[illegible]	69	72	61	78	47
46	46	46	44	48	57	44	42	46	58	58	72	78	40	44	79	78	73	77	71	44	79	[illegible]	68	65	57	58	47
-	99	100	83	76	42	45	43	99	47	47	47	46	73	83	47	43	48	45	46	83	47	[illegible]	49	48	42	47	79
	-	99	84	77	43	46	44	100	47	47	47	46	74	84	47	43	48	45	46	84	47	83	49	48	43	47	80
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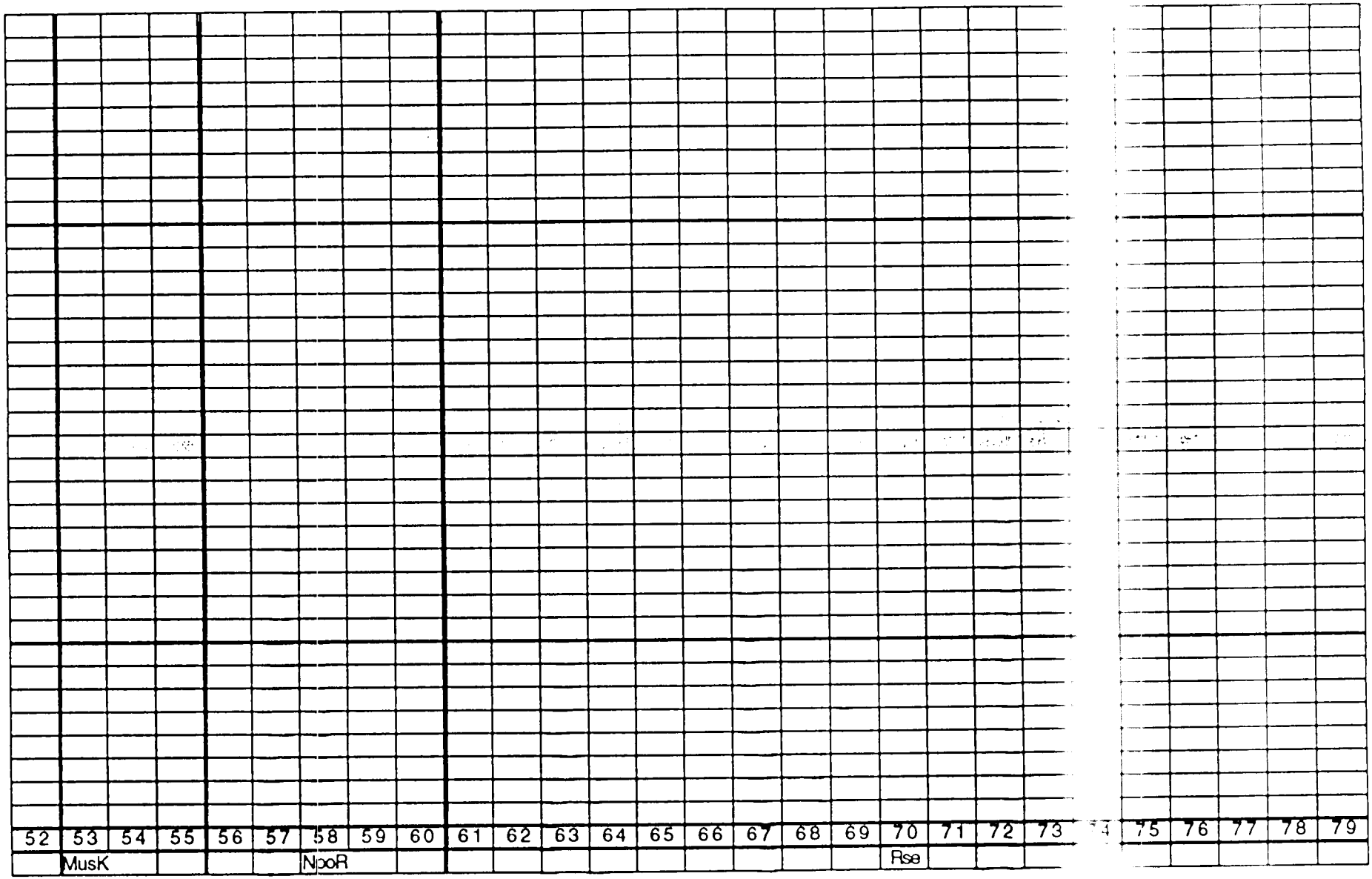
							-	44	45	46	47	46	41	46	47	43	48	46	46	46	47	46	49	46	48	46	45
								-	47	47	47	46	74	84	47	43	48	45	46	84	47	83	49	48	43	47	80
									-	100	66	65	43	47	66	60	67	64	66	47	66	46	66	78	59	100	46
										-	67	65	42	47	66	60	68	64	66	47	66	46	67	79	60	100	46
											-	88	41	46	89	86	97	87	96	46	89	45	82	75	60	67	46
												-	40	45	99	94	90	99	88	45	99	44	82	72	60	65	48
													-	88	41	43	42	40	41	88	41	88	44	43	40	42	72
														-	46	43	47	44	45	100	46	99	49	49	44	47	81
															-	95	90	98	88	46	100	45	83	73	61	66	49
																-	85	95	85	43	95	43	78	71	54	60	46
																	-	89	97	47	90	46	83	75	61	68	47
																		-	88	44	98	43	81	71	59	64	47
																			-	45	88	44	81	74	59	66	45
																				-	46	[illegible]	49	49	44	47	81
																					-	[illegible]	83	73	61	66	49
																							48	48	43	46	81
																							-	81	64	67	51
																								-	59	79	49
																									-	60	44
																										-	46
																											-



APPENDIX ~~-9-~~ Table 6.9

						Her3																ObR					
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	-	81	85	49	45	84	46	85	47	44	85	47	84	83	45	47	83	81	81	81	83	8	3	81	47	49	82	84
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APPENDIX ~~II~~ = Table C. 11

			-	53	48	86	47	100	50	45	100	50	87	85	49	50	85	85	85	85	85	85	50	52	85	86
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					-	47	59	48	60	60	48	60	47	48	77	60	47	47	47	47	47	47	60	67	46	47
						-	46	86	47	43	86	47	99	95	45	47	99	80	80	80	98	80	47	48	97	100
							-	47	76	61	47	76	46	48	65	76	46	48	48	48	45	48	76	76	45	46
								-	50	45	100	50	87	85	49	50	85	85	85	85	85	85	50	52	85	86
									-	60	50	100	47	48	72	100	47	46	46	46	47	46	100	75	46	47
										-	45	60	43	44	63	60	43	44	44	44	43	44	60	61	42	43
											-	50	87	85	49	50	85	85	85	85	85	85	50	52	85	86
												-	47	48	72	100	47	46	46	46	47	46	100	75	46	47
													-	94	45	47	98	79	79	79	97	79	47	48	96	99
														-	47	48	94	82	82	82	93	82	48	50	92	95
															-	72	45	48	48	48	45	48	72	77	44	45
																-	47	46	46	46	47	46	100	75	46	47
																	-	79	79	79	97	79	47	48	96	99
																		-	100	100	79	100	46	50	78	80
																			-	100	79	100	46	50	78	80
																				-	79	100	46	50	78	80
																					-	79	47	48	95	98
																						80	47	48	96	99
																						-	46	50	78	80
																							-	75	46	47
																								-	47	48
																									-	97
																										-
80	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100	101	102	103	104	105	106	107
						Her3															ObR						

					VEGF						
108	109	110	111	112	113	114	115	116	117		Clone
44	49	85	80	80	44	48	49	85	85	1	Axl.25
59	70	51	47	47	58	70	71	52	51	2	Axl.26
61	72	52	48	48	60	71	73	53	52	3	Axl.27
44	46	85	84	84	44	48	46	83	85	4	Axl.32
48	52	83	78	78	48	51	52	83	83	5	Axl.35
43	47	85	99	99	43	46	47	84	85	6	Axl.36
48	52	84	79	79	48	50	52	83	84	7	Axl.47
58	64	49	48	48	58	77	64	50	49	8	Axl.51
63	66	50	48	48	62	72	66	51	50	9	Axl.75
61	99	49	47	47	61	66	100	50	49	10	Axl.78
45	48	95	85	85	45	50	48	95	95	11	Axl.80
62	84	47	47	47	62	65	85	48	47	12	Axl.82
43	47	86	100	100	43	46	47	85	86	13	GCSFR.3.2E.A1
58	94	46	44	44	58	62	95	47	46	14	GCSFR.3.2E.D5
62	89	49	47	47	62	66	90	50	49	15	GCSFR.3.2E.D6
98	58	43	42	42	97	59	59	44	43	16	GCSFR.3.2E.G5
91	57	44	42	42	90	57	58	45	44	17	GCSFR.3.3E.C4
100	60	45	43	43	99	61	61	46	45	18	GCSFR.A2
61	99	49	47	47	61	66	100	50	49	19	GCSFR.A4
60	71	52	48	48	59	70	72	53	52	20	GCSFR.A5
61	72	52	48	48	60	71	73	53	52	21	GCSFR.A8
43	45	83	82	82	43	47	45	81	83	22	GCSFR.F7
61	94	51	49	49	61	69	94	52	51	23	GCSFR.G3
100	60	45	43	43	99	61	61	46	45	24	IgE.D8
43	47	86	99	99	43	46	47	85	86	25	IgE.G2
100	60	45	43	43	99	61	61	46	45	26	IgER.1A12
61	80	49	48	48	61	62	80	50	49	27	IgER.1D11
99	59	45	43	43	98	60	60	46	45	28	IgER.1E10
61	99	49	47	47	61	66	100	50	49	29	IgER.MAT2C1G11
99	59	47	45	45	98	60	60	46	47	30	Mpl.01
88	56	46	43	43	87	55	57	45	46	31	Mpl.02
100	58	46	44	44	99	60	59	46	46	32	Mpl.03
43	47	85	99	99	43	46	47	85	85	33	Mpl.04
72	78	49	47	47	72	67	79	50	49	34	Mpl.05
45	50	85	80	80	45	49	50	85	85	35	Mpl.06
67	66	51	48	48	66	76	66	54	51	36	Mpl.07
59	83	49	47	47	59	65	84	50	49	37	Mpl.08
44	48	84	95	95	44	46	48	83	84	38	Mpl.11
40	43	83	96	96	40	44	43	83	83	39	Mpl.12
44	46	85	84	84	44	48	46	83	85	40	Mpl.14

Table 6.13

44	46	84	83	83	44	49	46	83	84	41	Mpl.16
62	82	48	46	46	62	65	83	49	48	42	Mpl.19
43	47	86	100	100	43	46	47	85	86	43	Mpl.21
44	48	86	100	100	44	48	48	85	86	44	Mpl.24
61	96	50	48	48	61	69	97	51	50	45	Mpl.26
44	46	84	83	83	44	48	46	82	84	46	Mpl.28
54	61	44	43	43	54	94	61	47	44	47	Mpl.29
59	65	49	46	46	59	78	65	50	49	48	Mpl.30
60	66	50	47	47	60	79	66	51	50	49	Mpl.31
61	65	46	45	45	61	99	65	48	46	50	Mpl.32
57	78	47	46	46	57	60	79	49	47	51	Mpl.33
42	47	85	99	99	42	46	47	84	85	52	Mpl.35
43	47	86	100	100	43	46	47	85	86	53	MusK.01
42	47	85	99	99	42	46	47	84	85	54	MusK.02
44	46	85	84	84	44	48	46	83	85	55	MusK.06
46	49	80	77	77	46	50	49	78	80	56	NpoR.25
100	60	45	43	43	99	61	61	46	45	57	NpoR.44
49	48	48	46	46	49	45	48	49	48	58	NpoR.53
48	47	46	44	44	48	46	47	48	46	59	NpoR.81
43	47	86	100	100	43	46	47	85	86	60	NpoR.86
59	66	50	47	47	59	78	66	51	50	61	Rse.01
60	66	50	47	47	60	79	66	51	50	62	Rse.02
60	88	48	47	47	60	65	89	49	48	63	Rse.03
60	98	48	46	46	60	65	99	49	48	64	Rse.04
40	41	75	74	74	40	44	41	80	75	65	Rse.07
44	46	85	84	84	44	48	46	83	85	66	Rse.08
61	99	49	47	47	61	66	100	50	49	67	Rse.15
54	94	45	43	43	54	62	95	46	45	68	Rse.16
61	90	49	48	48	61	66	90	50	49	69	Rse.18
59	97	47	45	45	59	64	98	48	47	70	Rse.20
59	88	47	46	46	59	65	88	48	47	71	Rse.21
44	46	85	84	84	44	48	46	83	85	72	Rse.22
61	99	49	47	47	61	66	100	50	49	73	Rse.23
43	45	84	83	83	43	48	45	83	84	74	Rse.24
64	82	51	49	49	63	70	83	52	51	75	Rse.52
59	72	52	48	48	59	73	73	53	52	76	Rse.53
100	60	45	43	43	99	61	61	46	45	77	Rse.58
60	66	50	47	47	60	79	66	51	50	78	Rse.60
44	49	85	80	80	44	48	49	85	85	79	Rse.61
59	65	49	46	46	59	78	65	50	49	80	Rse.63
44	46	85	84	84	44	48	46	83	85	81	her3.1
44	49	85	80	80	44	48	49	85	85	82	her3.10

45	49	100	86	86	45	47	49	99	100	83	her3.11
65	75	53	49	49	64	73	76	54	53	84	her3.12
60	79	48	47	47	60	61	80	49	48	85	her3.16
43	47	86	100	100	43	46	47	85	86	86	her3.18
61	62	47	46	46	60	75	62	49	47	87	her3.19
45	49	100	86	86	45	47	49	99	100	88	her3.22
60	66	50	47	47	60	79	66	51	50	89	her3.3
100	60	45	43	43	99	61	61	46	45	90	her3.4
45	49	100	86	86	45	47	49	99	100	91	her3.7
60	66	50	47	47	60	79	66	51	50	92	obr.1
43	47	87	99	99	43	46	47	86	87	93	obr.11
44	49	85	95	95	44	48	49	83	85	94	obr.12
63	91	49	45	45	63	66	92	51	49	95	obr.14
60	66	50	47	47	60	79	66	51	50	96	obr.15
43	47	85	99	99	43	46	47	84	85	97	obr.16
44	49	85	80	80	44	48	49	85	85	98	obr.17
44	49	85	80	80	44	48	49	85	85	99	obr.18
44	49	85	80	80	44	48	49	85	85	100	obr.19
43	47	85	98	98	43	46	47	83	85	101	obr.2
43	47	86	99	99	43	46	47	85	86	102	obr.20
44	49	85	80	80	44	48	49	85	85	103	obr.21
60	66	50	47	47	60	79	66	51	50	104	obr.22
61	72	52	48	48	60	71	73	53	52	105	obr.23
42	46	85	97	97	42	45	46	83	85	106	obr.24
43	47	86	100	100	43	46	47	85	86	107	obr.26
-	60	45	43	43	99	61	61	46	45	108	obr.3
	-	49	47	47	60	66	99	50	49	109	obr.4
		-	86	86	45	47	49	99	100	110	vegf.1
			-	100	43	46	47	85	86	111	vegf.10
				-	43	46	47	85	86	112	vegf.2
					-	61	61	46	45	113	vegf.3
						-	66	49	47	114	vegf.4
							-	50	49	115	vegf.5
								-	99	116	vegf.6
									-	117	vegf.8
108	109	110	111	112	113	114	115	116	117		Clone
					VEGF						

In the Claims:

Claims 1-11, 15, 19-30 and 32 have been cancelled.

Claims 34-38 have been added.

Claims 12-14, 16, 31, and 33 have been amended as follows:

12. (Amended) A multispecific antibody prepared by the method [of claim 1] comprising:

(a) expressing in a host cell a first polypeptide comprising a first heavy chain variable domain, a first or second light chain variable domain, and a first multimerization domain, wherein the first and second light chain variable domains have at least 80% amino acid sequence identity, and wherein a first binding domain is formed by the first heavy chain variable domain and the first or second light chain variable domain;

(b) expressing in the host cell a second polypeptide comprising a second heavy chain variable domain, the first or the second light chain variable domain, and a second multimerization domain, wherein a second binding domain is formed by the second heavy chain variable domain and the first or second light chain variable domain, and wherein the first and second binding domains bind different antigens;

(c) allowing the first and second polypeptides to dimerize by interaction of the first and second multimerization domains to form a multispecific antibody; and

d) recovering the multispecific antibody from the host cell.

13. (Amended) A multispecific antibody comprising a first polypeptide and at least one additional polypeptide [which meet at an interface, wherein], the multispecific antibody comprising:

[(a) the first polypeptide comprises a multimerization domain

additional polypeptides comprise a common sequence]

(a) the first polypeptide which comprises a first heavy chain variable domain, a first or second light chain variable domain, and a first multimerization domain, wherein the first and second light chain variable domains have at least 80% amino acid sequence identity, and wherein a first binding domain is formed by the first heavy chain variable domain and the first or second light chain variable domain;

(b) the second polypeptide which comprises a second heavy chain variable domain, the first or the second light chain variable domain, and a second multimerization domain, wherein a second binding domain is formed by the second heavy chain variable domain and the first or second light chain variable domain, and wherein the first and second binding domains bind different antigens;

(c) the first and second polypeptides dimerize by interaction of the first and second multimerization domains to form a multispecific antibody.

14. (Amended) The multispecific antibody of claim 13, wherein the nucleic acid encoding the first polypeptide or the nucleic acid encoding the additional polypeptide, or both, has been altered from the original nucleic acid to encode the [interface] multimerization domain or a portion thereof.

16. (Amended) The multispecific antibody of claim 14 wherein the [interface of the] multimerization domains of the first and an additional polypeptide comprise a protuberance and cavity, respectively.

31. (Amended) The multispecific antibody of claim 13 [selected from the group consisting of] wherein the antibody is anti-Ob-R/anti-[illegible].

34. (New) The multispecific antibody of claim 13, wherein the first and second light chain variable domains have at least 90% amino acid sequence identity.

35. (New) The multispecific antibody of claim 13, wherein the first and second light chain variable domains have at least 95% amino acid sequence identity.

36. (New) The multispecific antibody of claim 13, wherein the first and second light chain variable domains have at least 98% amino acid sequence identity.

37. (New) The multispecific antibody of claim 13, wherein the first and second light chain variable domains have at least 99% amino acid sequence identity.

38. (New) The multispecific antibody of claim 13, wherein the first and second light chain variable domains have identical amino acid sequences.